

Remarks

Claims 1-11 were previously pending in the subject application. By this Amendment, claim 3 has been amended. Support for this amendment can be found throughout the specification and the claims as originally filed. Accordingly, claims 1-11 are now before the Examiner for consideration.

The amendment to claim 3 has been made in an effort to lend greater clarity to the claimed subject matter and to expedite prosecution. This amendment should not be taken to indicate the applicants' agreement with, or acquiescence to, the rejections of record. Favorable consideration of the claims now presented, in view of the remarks and amendments set forth herein, is earnestly solicited.

Claim 3 has been objected to under 35 U.S.C. §112, second paragraph, as being indefinite. The applicants have amended claim 3 to delete reference to "analogue," thereby rendering moot this ground for objection.

Claims 1-6 and 8-11 have been rejected under 35 U.S.C. §102(b) as being anticipated by Blaschke *et al.* (Archiv der Pharmazie, 1987, 320(4), 341—7, abstract). The applicants respectfully traverse this ground for rejection because the cited reference does not disclose the applicants' claimed process for increasing the optical purity of a mixture of enantiomers of nefopam wherein the process proceeds via the formation of a bisnefopam salt.

The Blaschke *et al.* reference discloses a process for the resolution of nefopam which, unlike the process of the current invention, proceeds via formation of the monotartrate salt.

It is a basic premise of patent law that, in order to anticipate, a single prior art reference must disclose within its four corners, each and every element of the claimed invention. In *Lindemann v. American Hoist and Derrick Co.*, 221 USPQ 481 (Fed. Cir. 1984), the court stated:

Anticipation requires the presence in a single prior art reference, disclosure of each and every element of the claimed invention, arranged as in the claim. *Connell v. Sears Roebuck and Co.*, 722 F.2d 1542, 220 USPQ 193 (Fed. Cir. 1983); *SSIH Equip. S.A. v. USITC*, 718 F.2d 365, 216 USPQ 678 (Fed. Cir. 1983). In deciding the issue of anticipation, the [examiner] must identify the elements of the claims, determine their meaning in light of the specification and prosecution history, and identify corresponding elements disclosed in the

allegedly anticipating reference. *SSIH, supra; Kalman [v. Kimberly-Clarke]*, 713 F.2d 760, 218 USPQ 781 (Fed. Cir. 1983)] (emphasis added). 221 USPQ at 485.

As noted above, Blaschke *et al.* disclose resolution of nefopam by a process that proceeds via formation of the monotartrate salt rather than through a bisnefopam salt, as is required by the applicants' claims.

The literature method prepares the monotartrate salt whereas the novel method prepares the bisnefopam tartrate salt (hemitartrate). Results show that the latter has clear advantages: it is more scaleable, uses lower volumes of solvent, does not use DMSO, requires only 0.25 equivalents of resolving agent, requires only one recrystallisation, and gives a better enantiomeric excess of the final product.

With regard to the rejection of claims 10 and 11, Blaschke *et al.* do not disclose the formation of the bisnefopam salt (see Example 5 of the current applicants' specification). To the contrary, the prior art process would have produced only the mono(nefopam) salt.

The applicants respectfully point out that for a claim to be anticipated under the principles of inherency, the subject of a single prior art reference must necessarily function in accordance with the limitations of the process or method claimed. *In re King*, 801 F.2d 1324, 1326, 231 USPQ 136, 138 (Fed. Cir. 1986). Further,

the doctrine of inherency is available only when the prior inherent event can be established as a certainty. That an event may result from a given set of circumstances is not sufficient to establish anticipation. . . . A prior inherent event cannot be established based on speculation, or where a doubt exists (emphasis added). *Ethyl Molded Product Co. v. Betts Package Inc.*, 9 USPQ 2d 1001, 1032-33 (E.D. KY 1988).

In this case, the cited reference provides no reason to believe that the claimed bisnefopam salt is formed, and it cannot be said that it is formed as a certainty, as would be required for a rejection based on inherency.

Accordingly, the applicants respectfully request reconsideration and withdrawal of the rejection under §102(b).

Claims 1-9 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Rexall Drug and Chemical Co. (DE 1620198, published April 6, 1972), in view of Treiber *et al.* (U.S. Patent No. 4,269,833). The applicants respectfully traverse this ground for rejection because the cited references, either taken alone or in combination, do not disclose or suggest the applicants' advantageous process.

First, the skilled artisan would have had no reason for combining these two references. The skilled person would not consider resolution of the two compounds disclosed by Treiber *et al.* as analogous merely because they are both analgesic compounds (in this context, the function of the product is irrelevant) or because they both have heterocyclic components. Resolution is an empirical art at best. It would be more reasonable to consider the substituents around the respective chiral centers and, in this case, the substituents cannot all be considered analogous.

It is well established in the patent law that the mere fact that the purported prior art could have been modified or applied in some manner to yield an applicant's invention does not make the modification or application obvious unless "there was an apparent reason to combine the known elements in the fashion claimed" by the applicant. *KSR International Co. v. Teleflex Inc.*, 550 U.S. \_\_\_\_ (2007). Furthermore, an applicant's invention is not "proved obvious merely by demonstrating that each of its elements was, independently, known in the (purported) prior art." *Id.* For a proper obviousness rejection, there must be some reason for the skilled artisan to combine the readings of the references. Here, there is no apparent reason.

Secondly, and perhaps more importantly, any combination that was made would suggest only that O,O-dibenzoyltartaric acid might be used as an agent for resolving nefopam. That resolution is already known, as disclosed by Blaschke *et al.* The present invention is distinct from a combination of Rexall and Treiber for the same reasons that it is distinct from Blaschke *et al.*

Specifically, as discussed above, the subject invention is based on the surprising discovery that racemic or non-racemic nefopam can be resolved more efficiently, using a substantially single enantiomer of O,O-dibenzoyltartaric acid or a related O,O-aroyltartaric

acid as a resolving agent, via formation of a novel bisnefopam tartrate (nefopam hemitartrate) salt.

As expressed by the CAFC, to support a §103 rejection, “[b]oth the suggestion and the expectation of success must be founded in the prior art ...” *In re Dow Chemical Co.* 5 USPQ 2d 1529, 1531 (Fed. Cir. 1988). An assertion of obviousness without the required suggestion or expectation of success in the prior art is tantamount to using applicant’s disclosure to reconstruct the prior art to arrive at the subject invention. Hindsight reconstruction of the prior art cannot support a §103 rejection, as was specifically recognized by the CCPA in *In re Sponnoble*, 56CCPA 823, 160 USPQ 237, 243 (1969).

The current applicants’ process is not only different from what is disclosed in the prior art, it is also surprisingly advantageous. Example 5 of the applicants’ specification shows the applicants’ process compared with the prior art process. The results show advantages in that the claimed process is more scaleable, uses lower volumes of solvent, does not use DMSO, requires only 0.25 equivalents of resolving agent, requires only one recrystallisation, and gives a better enantiomeric excess of the final product.

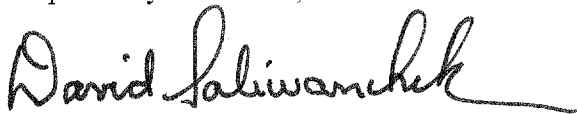
The prior art does not disclose or suggest the claimed process, or its significant advantages. Accordingly, the applicants respectfully request reconsideration and withdrawal of the rejection under §103(a).

In view of the foregoing remarks, the applicants believe that the currently pending claims are in condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge any fees under 37 CFR §§1.16 or 1.17 as required by this paper to Deposit Account No. 19-0065.

The applicants also invite the Examiner to call the undersigned if clarification is needed on any of this response, or if the Examiner believes a telephone interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,

A handwritten signature in black ink, reading "David R. Saliwanchik". The signature is fluid and cursive, with a long horizontal flourish extending to the right.

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